0013760372 BIOSIS NO.: 200200353883
A novel murine model of allogeneic vaccination against prostate cancer
AUTHOR: Labarthe Marie-Christine (Reprint); Thraves Peter; Theocharous Pantelli; Dalgleish Angus (Reprint); Whelan Mike
AUTHOR ADDRESS: Oncology, St. George's Hospital Medical School, Cranmer Terrace, London, SW17 0RE, UK**UK
JOURNAL: FASEB Journal 16 (4): pA333 March 20, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002; 20020420
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The development of allogeneic whole cell vaccines for prostate cancer is complicated by the lack of a relevant animal model. The murine system is most attractive as it allows for high throughput and allogenicity can easily be investigated. However, the lack of murine prostatic lines has hampered development. The prostate was removed from a male C3H (H-2k) mouse and cells transformed with an E6/E7 construct from HPV-18. The resulting line (PMC-1) was positive for cytokeratin 18, vimentin and androgen receptor and negative for desmin by immunohistochemistry. Androgen receptor was upregulated by culturing the cells in testosterone. Flow cytometry revealed a high level of MHC I expression, as well as CD80 and CD54. PMC-1 did not form tumours in nude mice. Female C57 (H-2b) mice were vaccinated with **irradiated** PMC-1 subcutaneously and challenged with syngeneic **prostate** tumour **cell line** RM9. Vaccinated animals showed a clear survival benefit. Initial investigation revealed high levels of NK activity and low CTL activity in vaccinated mice. This is in marked contrast to the murine B16 melanoma model and may suggest that T-cell activation is difficult to achieve in the prostate.

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? ds

Set      Items   Description
S1        8614   PROSTATE(5N)CELL(W)LINE??
S2      466682   IRRADIAT? OR KILLED
S3         209   S1 AND S2
S4     4909704   VACCINE OR TREAT?
S5         116   S3 AND S4
S6     1395146   CANCER OR ADENOCARCINOMA
S7         114   S5 AND S6
S8          60   RD (unique items)
? s (irradiated or killed)(5n)(prostate) (5n) (cell(w)line??)
Processing
          138169  IRRADIATED
           81815  KILLED
          163566  PROSTATE
         5018021  CELL
         2767444  LINE??
      S9      18  (IRRADIATED OR KILLED)(5N)(PROSTATE) (5N) (CELL(W)LINE??)
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S10       8  RD (unique items)
? t s10/3,k,ab/1-8

 10/3,K,AB/1      (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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15730917   PMID: 14985701
  Curcumin confers radiosensitizing effect in prostate cancer cell line
PC-3.
  Chendil Damodaran; Ranga Rama S; Meigooni David; Sathishkumar Sabapathi;
Ahmed Mansoor M
  Department of Clinical Science, University of Kentucky, Lexington, KY
40536, USA. dchen2@uky.edu
  Oncogene (England)  Feb 26 2004,  23  (8)  p1599-607,  ISSN 0950-9232
Journal Code: 8711562
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: In Process
  Curcumin (Diferuloylmethane) is a major chemical component of turmeric
(curcuma longa) and is used as a spice to give a specific flavor and yellow
color in Asian food. Curcumin exhibits growth inhibitory effects in a broad
range of tumors as well as in TPA-induced skin tumors in mice. This study
was undertaken to investigate the radiosensitizing effects of curcumin in
p53 mutant prostate cancer cell line PC-3. Compared to
cells that were irradiated alone (SF(2)=0.635; D(0)=231 cGy),
curcumin at 2 and 4 microM concentrations in combination with radiation
showed significant enhancement to radiation-induced clonogenic inhibition
(SF(2)=0.224: D(0)=97 cGy and SF(2)=0.080: D(0)=38 cGy) and apoptosis. It
has been reported that curcumin inhibits TNF-alpha-induced NFkappaB
activity that is essential for Bcl-2 protein induction. In PC-3 cells,
radiation upregulated TNF-alpha protein leading to an increase in NFkappaB
activity resulting in the induction of Bcl-2 protein. However, curcumin in
combination with radiation treated showed inhibition of TNF-alpha-mediated
NFkappaB activity resulting in bcl-2 protein downregulation. Bax protein
levels remained constant in these cells after radiation or curcumin plus
radiation treatments. However, the downregulation of Bcl-2 and no changes
in Bax protein levels in curcumin plus radiation-treated PC-3 cells,
together, altered the Bcl2 : Bax ratio and this caused the enhanced
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radiosensitization effect. In addition, significant activation of cytochrome c and caspase-9 and -3 were observed in curcumin plus radiation treatments. Together, these mechanisms strongly suggest that the natural compound curcumin is a potent radiosesitizer, and it acts by overcoming the effects of radiation-induced prosurvival gene expression in prostate cancer.

... mice. This study was undertaken to investigate the radiosensitizing effects of curcumin in p53 mutant **prostate** cancer **cell line** PC-3. Compared to cells that were **irradiated** alone (SF(2)=0.635; D(0)=231 cGy), curcumin at 2 and 4 microM...

10/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12962300 PMID: 8620475
Radiosensitizing effect of cisplatin in prostate cancer cell lines.
Geldof A A; Slotman B J
Department of Endocrinology/Urology, Free University Hospital, Amsterdam, The Netherlands.
Cancer letters (IRELAND) Mar 29 1996, 101 (2) p233-9, ISSN 0304-3835 Journal Code: 7600053
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The radiosensitizing effect of platinum compounds has been demonstrated in a number of tumors. In prostate cancer, clinical and preclinical data concerning an eventual efficacy of the concept of radiosensitization are lacking. In the present study cisplatin and carboplatin have been used as a model to explore radiosensitization in in vitro **prostate** cancer **cell lines**. Human (DU-145) and rat (R3327-MATLyLu) **prostate** tumor cells were **irradiated** with doses ranging from 0 to 8 Gy in the presence of various concentrations of either cisplatin or carboplatin. For the evaluation of the combined effect of the two treatment modalities, a simple model is presented. Supra-additive treatment effects of combinations of platinum drugs with radiotherapy, both at clinically achievable doses, were shown on the basis of surviving fractions of tumor cells and proved to be significant. These data strongly suggest that radiotherapy may be effectively combined with radiosensitizers such as platinum drugs in prostate cancer therapy, to yield synergism in treatment efficacy.

... cisplatin and carboplatin have been used as a model to explore radiosensitization in in vitro **prostate** cancer **cell lines** . Human (DU-145) and rat (R3327-MATLyLu) **prostate** tumor cells were **irradiated** with doses ranging from 0 to 8 Gy in the presence of various concentrations of...

10/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12494883 PMID: 12957250
Incorporating clinical measurements of hypoxia into tumor local control modeling of prostate cancer: implications for the alpha/beta ratio.
Nahum Alan E; Movsas Benjamin; Horwitz Eric M; Stobbe Corinne C; Chapman J Donald
Department of Radiation Oncology, Fox Chase Cancer Center, Philadelphia, PA 19111, USA.
International journal of radiation oncology, biology, physics (United

States) Oct 1 2003, 57 (2) p391-401, ISSN 0360-3016 Journal Code: 7603616
Contract/Grant No.: CA06927; CA; NCI; CA41078; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BACKGROUND AND PURPOSE: The recently obtained low value of approximately 1.5 for the alpha/beta of prostate cancer has led us to reexamine the optimal prostate tumor biology parameters, while taking into account everything known about the radiation response of prostate clonogens for use in a predictive dose-response model. METHODS AND MATERIALS: Averages of the literature values of the alpha- and beta-inactivation coefficients for human prostate cancer cell lines were calculated. A robust tumor local control probability (TLCP) model was used that required average alpha and beta, as well as sigma(alpha), for the interpatient variation in single-hit killing (alpha). Median PO(2) values <or=1 mm Hg in the prostates of Fox Chase Cancer Center brachytherapy patients had been found in 21% of 115 cases. The oxygen enhancement ratios of 1.75 and 3.25 for alpha- and beta-inactivation, respectively, measured for tumor cells in vitro, were incorporated into the TLCP model, together with a clonogen density of approximately 10(5) cells/cm(3). Severe hypoxia and radioresistance were estimated for a proportion of tumors that was increased with PSA level. RESULTS: For asynchronous human **prostate cell lines irradiated** in air, alpha(mean) was 0.26 +/- 0.07 (standard error) Gy(-1), sigma(alpha) = 0.06 Gy(-1), and beta(mean) was 0.0312 Gy(-2) +/- 0.0064 (standard error) Gy(-2). The TLCP data indicated that most tumors that contained aerobic cells would be cured, whereas most tumors that contained hypoxic cells would not be cured by total doses of 76 to 80 Gy. Clinical response data from the literature for external beam dose escalation, stratified by PSA value, and for low-dose-rate brachytherapy, were well predicted by the model, where the alpha/beta ratio was 8.5 and 15.5 for well-oxygenated and hypoxic clonogens, respectively. CONCLUSIONS: Neither alpha/beta ratio nor clonogen number need be extremely low to explain the response of prostate cancer to brachytherapy and external beam therapy, contradicting other recent analyses. It is strongly suggested that severe hypoxia in the prostates of certain patients limits the overall cancer cure rate by conventional radiation therapy.

...for a proportion of tumors that was increased with PSA level. RESULTS: For asynchronous human **prostate cell lines irradiated** in air, alpha(mean) was 0.26 +/- 0.07 (standard error) Gy(-1), sigma(alpha...

10/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12307675 PMID: 12665684
Serum markers variation consistent with autoschizis induced by ascorbic acid-menadione in patients with prostate cancer.
Lasalvia-Prisco Eduardo; Cucchi Silvia; Vazquez Jesus; Lasalvia-Galante Eduardo; Golomar Wilson; Gordon William
School of Medicine, University of Uraguay, Montevideo, Uriguay. telemedical@pharmablood.com
Medical oncology (Northwood, London, England) (United States) 2003, 20 (1) p45-52, ISSN 1357-0560 Journal Code: 9435512
Document type: Clinical Trial; Journal Article; Multicenter Study; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In vitro exposure of malignant **prostate cell lines** to

ascorbic acid-menadione showed that tumor cells were **killed** through a mechanism named autoschizis. Experimental animal studies showed that autoschizis is also evident when ascorbic acid-menadione is administered to nude mice with implanted human prostate tumors. Prostate-specific antigen (PSA) is a known serum marker of prostate tumor cells specific activity. Recently, total serum homocysteine has been identified as a marker of tumor cell numbers with sensitivity for early detection of tumor cell death induced by treatments. A clinical trial with prostate cancer patients submitted to the association of ascorbic acid-menadione was performed and PSA/homocysteine was assessed in the follow- up. The early response in serum PSA and homocysteine levels was reported. The results showed that ascorbic acid-menadione produced an immediate drop in tumor cell numbers as assessed by homocysteine levels. Serum PSA levels showed an early rise and later dropped. These results suggest that autoschizis can also be induced by this pharmacological association at the clinical level in prostate cancer patients. Further studies are being performed in order to research if these results can be found with other primary tumors as it was shown in in vitro and experimental models. Ascorbic acid-menadione could be emerging as a new antitumoral chemotherapy.

In vitro exposure of malignant **prostate cell lines** to ascorbic acid-menadione showed that tumor cells were **killed** through a mechanism named autoschizis. Experimental animal studies showed that autoschizis is also evident when...

10/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11683910 PMID: 11857034

Resistance of prostate cancer cells to soluble TNF-related apoptosis-inducing ligand (TRAIL/Apo2L) can be overcome by doxorubicin or adenoviral delivery of full-length TRAIL.

Voelkel-Johnson Christina; King Deanne Lea; Norris James Scott

Department of Microbiology and Immunology, Medical University of South Carolina, Charleston, South Carolina 29425, USA. johnsocv@musc.edu

Cancer gene therapy (England) Feb 2002, 9 (2) p164-72, ISSN 0929-1903 Journal Code: 9432230

Contract/Grant No.: R01 CA69596; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL/Apo2L) has been shown to induce apoptosis in malignant cells without harming normal cells. To determine the antitumor potential of TRAIL against prostate cells, we undertook a comprehensive study that included eight prostate cancer cells lines (CWR22Rv1, Du145, DuPro, JCA-1, LNCaP, PC-3, PPC-1, and TsuPr1) and primary cultures of normal prostate epithelial cells (PrEC). Cells were tested for susceptibility to soluble TRAIL in the presence or absence of the chemotherapeutic agent doxorubicin. TRAIL was also delivered by an adenoviral vector. Our results reveal that Du145, DuPro, LNCap, TsuPr1, and PrEC were resistant to 100 ng/mL TRAIL. JCA-1 and PPC-1 were slightly sensitive (20% killing) and PC-3 and CWR22Rv1 exhibited the highest sensitivity to TRAIL (30% and 50% killing, respectively). The combination of 10 ng/mL TRAIL with doxorubicin resulted in 60-80% cytotoxicity in seven of eight prostate cancer cells. TRAIL-mediated apoptosis involved cleavage of Bid, caspase-3, and PARP, and required caspase-8 and -9 activity. Full-length TRAIL delivered by an adenoviral vector (AdTRAIL-IRES-GFP) **killed prostate** cancer **cell lines** and PrEC without requisite doxorubicin cotreatment. Therefore, expression of the transgene from a tissue-specific promotor would make gene therapy with AdTRAIL-IRES-GFP a possibility.

...8 and -9 activity. Full-length TRAIL delivered by an adenoviral vector (AdTRAIL-IRES-GFP) **killed prostate** cancer **cell lines** and PrEC without requisite doxorubicin cotreatment. Therefore, expression of the transgene from a tissue-specific...

10/3,K,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11388851 PMID: 11482451
Chemosensitivity of prostatic tumour cell lines under conditions of G2 block abrogation.
Serafin A M; Binder A B; Bohm L
Department of Radiation Oncology, University of Stellenbosch Medical Faculty, Tygerberg, South Africa.
Urological research (Germany) Jun 2001, 29 (3) p221-7, ISSN 0300-5623 Journal Code: 0364311
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Conventional chemotherapy has had very limited success in the control of hormone-refractory prostate cancer. Methylxanthine derivatives, such as pentoxifylline (PTX), are known to abrogate the G2 block and enhance the toxicity of ionising irradiation and chemotherapeutic agents. It is now also established that late addition of the cytotoxic drug after irradiation under conditions of G2 block abrogation sensitises human tumour cells for cytotoxins. Here we assess whether the chemosensitivity of prostate tumour cell lines can be enhanced by the application of a low dose of drug in conjunction with a G2 block abrogator. **Prostate cell lines** DU145, BM1604 and LNCaP were **irradiated** with 7 Gy 60Co gamma-irradiation. A sub-toxic (2 mM) dose of pentoxifylline and a cytotoxic drug were added at maximum expression of the G2 cell cycle block and cell survival was determined by colony assay. Cisplatin, etoposide and vinblastine were tested at a toxic dose of 10% (TD10). In the TP53 mutant cell lines, DU145 and BM1604, dose enhancement factors (EFs) were found to be in the region of 4.20 for cisplatin, 3.70 for vinblastine, and 3.20 for etoposide. In the TP53 wild-type cell line, LNCaP, the enhancement factors were low and in the region of 1.20 for cisplatin, vinblastine and etoposide. It is clear, therefore, that toxicity enhancement factors (EFs) are greater in the TP53 mutant cell lines, DU145 and BM1604, than in the TP53 wild-type cell line, LNCaP. The results indicate that a significant enhancement of drug toxicity can be obtained if the cytotoxic drug is given under conditions of G2 block abrogation. The sensitisation of prostate cancer cells to cytotoxic drugs is particularly high in radiation-resistant TP53 mutant tumour cells. Drugs which abrogate G2 block have the potential to enhance the therapeutic index and therefore reduce the toxicity of chemotherapy drugs.

... the application of a low dose of drug in conjunction with a G2 block abrogator. **Prostate cell lines** DU145, BM1604 and LNCaP were **irradiated** with 7 Gy 60Co gamma-irradiation. A sub-toxic (2 mM) dose of pentoxifylline and...

10/3,K,AB/7 (Item 1 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

0013760372 BIOSIS NO.: 200200353883
A novel murine model of allogeneic vaccination against prostate cancer
AUTHOR: Labarthe Marie-Christine (Reprint); Thraves Peter; Theocharous

Pantelli; Dalgleish Angus (Reprint); Whelan Mike
AUTHOR ADDRESS: Oncology, St. George's Hospital Medical School, Cranmer Terrace, London, SW17 0RE, UK**UK
JOURNAL: FASEB Journal 16 (4): pA333 March 20, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002; 20020420
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The development of allogeneic whole cell vaccines for prostate cancer is complicated by the lack of a relevant animal model. The murine system is most attractive as it allows for high throughput and allogenicity can easily be investigated. However, the lack of murine prostatic lines has hampered development. The prostate was removed from a male C3H (H-2k) mouse and cells transformed with an E6/E7 construct from HPV-18. The resulting line (PMC-1) was positive for cytokeratin 18, vimentin and androgen receptor and negative for desmin by immunohistochemistry. Androgen receptor was upregulated by culturing the cells in testosterone. Flow cytometry revealed a high level of MHC I expression, as well as CD80 and CD54. PMC-1 did not form tumours in nude mice. Female C57 (H-2b) mice were vaccinated with **irradiated** PMC-1 subcutaneously and challenged with syngeneic **prostate** tumour **cell line** RM9. Vaccinated animals showed a clear survival benefit. Initial investigation revealed high levels of NK activity and low CTL activity in vaccinated mice. This is in marked contrast to the murine B16 melanoma model and may suggest that T-cell activation is difficult to achieve in the prostate.

...ABSTRACT: did not form tumours in nude mice. Female C57 (H-2b) mice were vaccinated with **irradiated** PMC-1 subcutaneously and challenged with syngeneic **prostate** tumour **cell line** RM9. Vaccinated animals showed a clear survival benefit. Initial investigation revealed high levels of NK...

10/3,K,AB/8 (Item 2 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

0013024851 BIOSIS NO.: 200100196690
Adenovirus-mediated transfer of inducible caspases: A novel "death switch" gene therapeutic approach to prostate cancer
AUTHOR: Shariat Shahrokh F; Desai Smruti; Song Weitao; Khan Tahira; Zhao Julie; Nguyen Cuong; Foster Barbara A; Greenberg Norman; Spencer David M (Reprint); Slawin Kevin M (Reprint)
AUTHOR ADDRESS: Scott Department of Urology, Baylor Prostate Center, Baylor College of Medicine, 6560 Fannin Street, STE 2100, Houston, TX, 77030, USA**USA
JOURNAL: Cancer Research 61 (6): p2562-2571 March 15, 2001 2001
MEDIUM: print
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In patients with localized prostate cancer, radical prostatectomy and radiation therapy, although effective in controlling localized disease, are often associated with significant side effects attributable to injury of adjacent tissues. Moreover, patients with metastatic disease

eventually fail systemic hormonal or chemotherapy because of the development of progressive, refractory disease. In this study, we evaluated the safety and efficacy of a novel suicide gene therapy that could potentially spare normal tissue while bypassing molecular mechanisms of apoptosis resistance by using chemically inducible effector caspases to trigger apoptosis in prostate cancer cells. Initially, we compared the ability of a panel of inducible Fas signaling intermediates to kill human and murine prostate cancer cell lines. On the basis of the superior killing by downstream caspase-1 and caspase-3, replication-deficient adenoviral vectors expressing conditional caspase-1 (Ad-G/iCasp1) or caspase-3 (Ad-G/iCasp3), regulated by nontoxic, lipid-permeable, chemical inducers of dimerization (CID), were constructed. Upon vector transduction followed by CID administration, aggregation and activation of these recombinant caspases occur, leading to rapid apoptosis. In vitro, both human (LNCaP and PC-3) and murine (TRAMP-C2 and TRAMP-C2G) **prostate** cancer **cell lines** were efficiently transduced and **killed** in a CID-dependent fashion. In vivo, direct injection of Ad-G/iCasp1 into s.c. TRAMP-C2 tumors caused focal but extensive apoptosis without evidence for a bystander effect at the maximal viral dose (i.e., 2.5 X 1010 viral particles/25 mul) in host animals that also received CID compared with control animals. Treatment with Ad-G/iCasp1 plus CID resulted in a transient, yet significant, reduction both in tumor growth and volume compared with tumors treated with vector but not CID ($P < 0.035$) or vector-diluent plus CID ($P < 0.022$), both of which grew more rapidly. These results demonstrate that CID-regulated, caspase-based suicide gene therapy is safe and can inhibit the growth of experimental prostate cancer in vitro and in vivo through potent induction of apoptosis, providing a rationale for further development.

...ABSTRACT: In vitro, both human (LNCaP and PC-3) and murine (TRAMP-C2 and TRAMP-C2G) **prostate** cancer **cell lines** were efficiently transduced and **killed** in a CID-dependent fashion. In vivo, direct injection of Ad-G/iCasp1 into s...

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